

CLAIMS

1. A method of determining susceptibility of a patient to developing a chronic ulcer, comprising determining the polymorphism type of the patient in genes that encode inflammatory cytokines.
2. A method of predicting the severity of a chronic ulcer in a patient comprising determining the polymorphism type of the patient in genes that encode inflammatory cytokines.
3. A method of predicting the healing response in a chronic ulcer in a patient comprising determining the polymorphism type of the patient for inflammatory cytokines.
4. A method according to any one of claims 1 to 3, wherein the chronic ulcer is a dermal ulcer.
5. A method according to claim 4, wherein the dermal ulcer is selected from the group consisting of venous ulcers, pressure sores and decubitus ulcers.
6. A method according to any one of claims 1 to ³ wherein the method is carried out *in vitro*.
7. A method according to ^{claim 1, 2, or 3} ~~any one of the previous claims~~ wherein the inflammatory cytokine comprises any one of interleukin 1, interleukin 6, interleukin 8 and tumour necrosis factor alpha.
8. The method according to claim 7, wherein the inflammatory cytokine comprises either of interleukin 1 or tumour necrosis factor alpha.
9. A method according to claim 8, wherein the presence of the +3953IL-1B polymorphism is diagnostic or prognostic for chronic ulcers.
10. A method according to claim 8, wherein the presence of the IL-1A -889 polymorphism is diagnostic or prognostic for chronic ulcers.
11. A method according to claim 8, wherein the presence of the +3953 IL-1B and the IL-1A -889 polymorphisms is diagnostic or prognostic for chronic ulcers.
12. The method of ^{claim 1, 2, or 3} ~~any preceding claim~~ wherein the analysis is carried out by:
 - (a) digesting genomic DNA from a patient to a diagnostic fragment length;
 - (b) probing the DNA fragment with a probe specific for a polymorphism type,
 and

- a
13. (c) detecting the bound probe.
The method of ~~any one of claims 1 to 11~~ ^{claim 1, 2, 10, 3}, comprising the following steps:
- 5 (a) amplifying a diagnostic length DNA fragment of an inflammatory cytokine from DNA samples isolated from patients,
- (b) probing the amplified DNA sample with a probe specific for an inflammatory cytokine polymorphism type and
- (c) detecting the bound probe.
- a 14. The method of ~~any one of claims 1 to 11~~ ^{claim 1, 2, 10, 3}, comprising the following steps:
- 10 (a) amplifying a diagnostic length DNA fragment of the gene encoding an inflammatory cytokine from DNA samples isolated from patients,
- (b) performing a second (nested) amplification to produce greater quantities of specific DNA, and
- (c) sequencing the amplified DNA fragment in order to analyse the precise polymorphism type of the gene.
- 15 15. The method according to ~~any one of claims 12 to 14~~ ^{claim 12} wherein the patient DNA is prepared from a blood sample.
16. The method according to ~~either of claims 12 or 13~~ ^{claim 12}, wherein the probe is detected using chemiluminescence.
17. The method according to ~~either of claims 12 or 13~~ ^{claim 12}, wherein the probe is detected by autoradiography.
- 20 18. Use of polymorphism typing for inflammatory cytokines in a method of determining susceptibility to, predicting the severity of and/or healing response of chronic ulcers in a patient.
19. ~~The method~~ ^{Use according to claim 18}, wherein said patient is a human patient.
- 25 20. A diagnostic kit for use in accordance with any one of the methods of ~~previous claims 1 to 15~~ ^{claim 1, 2, 10, 3} comprising a thermostable DNA polymerase enzyme, specific primers that are complementary to a gene encoding an inflammatory cytokine, ATP, mixed nucleotide units for extension of the nucleotide chain, and fluorescent-labelled dideoxynucleotide termination products.
- 30 21. A diagnostic kit for use in accordance with any one of the methods of ~~claims 1 to 15~~ ^{claims 1, 2, 10, 3} comprising a thermostable DNA polymerase enzyme, specific primers that are complementary to a gene encoding an inflammatory cytokine, ATP, mixed nucleotide units for extension of the nucleotide chain, a restriction enzyme

associated with a polymorphism associated with a gene encoding an inflammatory cytokine, a specific probe and concentrated forms of reagents and buffers useful in hybridisation, pre-hybridisation and DNA extraction.

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